In Vitro Fertilization Significantly Impacts the Female Placental Proteome in a Mouse Model

Lisa A. Vrooman[1], Josue Baeza[2], Eric A. Rhon-Calderon[2], Benjamin A. Garcia[3], Marisa S. Bartolomei[2]

1. Division of Reproductive and Developmental Sciences, Oregon National Primate Research Center, Oregon Health and Science University, Beaverton, OR
2. Department of Cell and Developmental Biology, Perelman School of Medicine, Epigenetics Institute, University of Pennsylvania, Philadelphia, PA
3. Department of Biochemistry and Molecular Biophysics, Washington University in St. Louis, St. Louis, MO

There is significant evidence that placental development is impacted in pregnancies conceived by assisted reproductive technologies (ART). Specifically, ART pregnancies have increased risk of preeclampsia, placental abruption, and morbidly adherent placentas. Abnormal placental morphology, specifically the developmental delay of placental vasculature and overgrowth of the endocrine compartment, impaired placental transport, reduced fetal weight, altered gene expression, and loss of DNA methylation have been robustly observed in a mouse model of in vitro fertilization (IVF). Identifying placental protein differences with IVF, pathological and compensatory, would help inform potential interventions for placental insufficiency as well as identify proteins that have a yet uncovered, but important role in placental development. We determined the placental protein abundance differences in IVF and spontaneously-conceived male and female mouse placentas by data-independent acquisition mass spectrometry at five timepoints (E11.5, 12.5, 14.5, 16.5, and 18.5). Proteome analyses were conducted on placentas (one male and one female closest to litter mean) from each litter (n=4-5 concepti/group/timepoint). Peptides below 1% FDR were used and statistical analysis was performed using Two-way ANOVA and Tukey HSD post hoc tests. All p-values reported were corrected for multiple hypothesis testing. Our results demonstrate placental proteins exhibit normal, dynamic change over placental development and that IVF induces an overall reduction in the abundance of several placental proteins at the earliest timepoint, E11.5. Several of the identified affected proteins are known to be important for placenta development. We further determined that placental protein levels are more affected in females. To our knowledge, this is the first proteomic analysis of mouse placentas at multiple timepoints along prenatal development. Thus, in addition to the insights into changes with IVF, this study provides a rich resource to understand protein abundance of proteins of interest over placental development for the research community.